FILE 'HOME' ENTERED AT 09:47:16 ON 07 JUN 2004

=> file biosis meldine caplus wpids uspatfull 'MELDINE' IS NOT A VALID FILE NAME Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files that are available. If you have requested multiple files, you can specify a corrected file name or you can enter "IGNORE" to continue accessing the remaining file names entered. ENTER A FILE NAME OR (IGNORE): medline

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FULL ESTIMATED COST

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FILE 'MEDLINE' ENTERED AT 09:47:40 ON 07 JUN 2004

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FILE 'WPIDS' ENTERED AT 09:47:40 ON 07 JUN 2004 COPYRIGHT (C) 2004 THOMSON DERWENT

FILE 'USPATFULL' ENTERED AT 09:47:40 ON 07 JUN 2004 CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

*** YOU HAVE NEW MAIL ***

=> s typ? (4a) (prion or spongiform) (4a) encephalopathy) UNMATCHED RIGHT PARENTHESIS 'PHALOPATHY)' The number of right parentheses in a query must be equal to the number of left parentheses.

=> s typ? (4a) (prion or spongiform) (4a) encephalopathy 61 TYP? (4A) (PRION OR SPONGIFORM) (4A) ENCEPHALOPATHY L1

=> s l1 and standard

11 L1 AND STANDARD

=> dup rem 12

PROCESSING COMPLETED FOR L2

11 DUP REM L2 (0 DUPLICATES REMOVED) L3

=> d 13 bib abs 1-11

ANSWER 1 OF 11 USPATFULL on STN L3

AN 2003:311783 USPATFULL

Compounds and methods for diagnosing and treating amyloid-related ${ t TI}$ conditions

Raub, Thomas J., Kalamazoo, MI, UNITED STATES INSawada, Geri A., Portage, MI, UNITED STATES Tanis, Steven P., Kalamazoo, MI, UNITED STATES Fici, Gregory J., Kalamazoo, MI, UNITED STATES Buhl, Allen Edwin, Portage, MI, UNITED STATES Carter, Donald Bainbridge, Kalamazoo, MI, UNITED STATES Bandiera, Tiziano, Gambolo-Pavia, ITALY Lansen, Jacqueline, Milan, ITALY Pellerano, Cesare, Siena, ITALY Savini, Luisa, Siena, ITALY

Pharmacia & Upjohn Company (U.S. corporation) PA

```
20031127
PI
      US 2003219377
                          A1
                               20030423 (10)
ΑI
      US 2003-421126
                          Α1
      Division of Ser. No. US 2000-667357, filed on 22 Sep 2000, GRANTED, Pat.
RLI
      No. US 6589504
PRAI
      US 2000-234611P
                           20000922 (60)
DT
      Utility
FS
      APPLICATION
      MARSHALL, GERSTEIN & BORUN LLP, 6300 SEARS TOWER, 233 S. WACKER DRIVE,
LREP
       CHICAGO, IL, 60606
      Number of Claims: 34
CLMN
      Exemplary Claim: 1
ECL
      No Drawings
DRWN
LN.CNT 1295
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The invention provides methods for diagnosing and treating
AB
       amyloid-related conditions and compounds useful for the same. The
       invention provides for detecting, imaging, monitoring, diagnosing, and
       treating conditions characterized by the binding or aggregation of
       amyloid fibrils. More particularly, the invention relates to using
       quinolinehydrazone compounds for diagnosing and treating amyloidotic
       conditions and also as an antioxidant.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L3
     ANSWER 2 OF 11 USPATFULL on STN
AN
       2003:306446 USPATFULL
       Motif-grafted hybrid polypeptides and uses thereof
TI
       Burton, Dennis R., La Jolla, CA, UNITED STATES
IN
       Moroncini, Gianluca, La Jolla, CA, UNITED STATES
       Williamson, R. Anthony, San Diego, CA, UNITED STATES
       US 2003215880
PI
                          A1
                               20031120
                               20030408 (10)
ΑI
       US 2003-410907
                          A1
       US 2002-371610P 20020409 (60)
PRAI
       Utility
DT
       APPLICATION
FS
       Stephanie Seidman, Heller Ehrman White & McAuliffe LLP, 7th Floor, 4350
LREP
       La Jolla Village Dr., San Diego, CA, 92122
       Number of Claims: 108
CLMN
       Exemplary Claim: 1
ECL
       4 Drawing Page(s)
DRWN
LN.CNT 4132
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Provided herein are hybrid polypeptides that specifically bind to a
       disease-associated isoform of a polypeptide involved in diseases of
       protein aggregation. The hybrid polypeptides can be used for diagnosis
       and treatment of such diseases. In a particular embodiment, a hybrid
       protein that specifically binds to the infectious form of a prion
       (PrP.sup.Sc) is provided.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L3
     ANSWER 3 OF 11 USPATFULL on STN
AN
       2003:299889 USPATFULL
       Pharmaceutical compositions and articles of manufacture useful in
TI
       reversal of a clinical epiosode of an incurable disease and methods of
       use thereof
       Shimoni, Zvi, Netanya, ISRAEL
IN
       Niven, Mark Jonathan, Bnei Brak, ISRAEL
       Bulvik, Shlomo, Kfar Haroeh, ISRAEL
       LANIADO KIRYAT SANZ HOSPITAL (non-U.S. corporation)
PA
       US 2003211110
PI
                          A1
                               20031113
                               20030416 (10)
ΑI
       US 2003-414011
                         A1
       US 2002-377953P 20020507 (60)
PRAI
```

 $\mathsf{D}\mathsf{T}$

Utility

FS APPLICATION

LREP DR. MARK FRIEDMAN LTD., C/o Bill Polkinghorn, Discovery Dispatch, 9003

Florin Way, Upper Marlboro, MD, 20772

CLMN Number of Claims: 20 ECL Exemplary Claim: 1 DRWN 1 Drawing Page(s)

LN.CNT 858

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of reversing a clinical episode of a disease which is generally considered incurable in a subject. The method includes providing an immune-globulin preparation containing a detectable titre of antibodies to the disease which is generally considered incurable and administering the immune-globulin preparation to the subject. Preferably, the immune globulin preparation is a pool of immune globulin fractions gathered from blood of donors living in an area where the disease is endemic. Further disclosed are pharmaceutical compositions and articles of manufacture suited for use in practice of the method.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 4 OF 11 USPATFULL on STN

AN 2003:213736 USPATFULL

Anti-abnormal type prion monoclonal antibody, process for producing the

same, and immunoassay using the same

IN Kurano, Yoshihiro, Chuo-ku, JAPAN

Umetani, Atsushi, Chuo-ku, JAPAN

Miyakoshi, Hideo, Chuo-ku, JAPAN

Yanagiya, Takayuki, Chuo-ku, JAPAN

PI US 2003148374 A1 20030807 AI US 2001-5120 A1 20011207 (10)

DT Utility

FS APPLICATION

LREP BIRCH STEWART KOLASCH & BIRCH, PO BOX 747, FALLS CHURCH, VA, 22040-0747

CLMN Number of Claims: 17

ECL Exemplary Claim: 1

DRWN 1 Drawing Page(s)

LN.CNT 567

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A monoclonal antibody which enables to distinguish the abnormal type prion from the normal type prion, as well as production process thereof, is disclosed. The anti-abnormal type prion monoclonal antibody of the invention reacts with abnormal type prion by antigen-antibody reaction but does not substantially react with normal type prion by antigen-antibody reaction. The anti-abnormal type prion monoclonal antibody of the invention may be obtained by immunizing an animal with an immunogen including a peptide containing a plurality of regions in the abnormal type prion, which regions are discontinuous each other in primary amino acid sequence of the abnormal type prion.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 5 OF 11 USPATFULL on STN

AN 2003:213245 USPATFULL

TI METHODS FOR AMYLOID REMOVAL USING ANTI-AMYLOID ANTIBODIES

IN SOLOMON, ALAN, KNOXVILLE, TN, UNITED STATES HRNCIC, RUDI, KNOXVILLE, TN, UNITED STATES

WALL, JONATHAN STUART, KNOXVILLE, TN, UNITED STATES

PI US 2003147882 Al 20030807

AI US 1999-316387 A1 19990521 (9)

PRAI US 1998-86198P 19980521 (60)

DT Utility

FS APPLICATION

LREP MORGAN LEWIS & BOCKIUS LLP, 1111 PENNSYLVANIA AVENUE NW, WASHINGTON, DC, 20004

```
Number of Claims: 22
CLMN
       Exemplary Claim: 1
ECL
       4 Drawing Page(s)
DRWN
LN.CNT 860
AB
```

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Methods and related immunoglobulin peptides and fragments thereof are disclosed that enhance the cell-mediated immune response of a patient to deposits of amyloid fibrils. These methods exploit the opsonizing effect of antibodies directed toward amyloid material or its component parts.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

```
L3
     ANSWER 6 OF 11 USPATFULL on STN
       2003:159842 USPATFULL
AN
       Multi-component antioxidant compounds, pharmaceutical compositions
TI
       containing same and their use for reducing or preventing oxidative
       stress
       Atlas, Daphne, Jerusalem, ISRAEL
IN
       Yissum Research Development Company of the Hebrew University of
PA
       Jerusalem (non-U.S. corporation)
       US 2003109457
                                20030612
PI
                           A1
                                20020905 (10)
AI
       US 2002-234319
                           A1
PRAI
       WO 2001-IL984
                            20011025
       Utility
DT
FS
       APPLICATION
LREP
       G.E. EHRLICH LTD., c/o ANTHONY CASTORINA, SUITE 207, 2001 JEFFERSON
       DAVIS HIGHWAY, ARLINGTON, VA, 22202
       Number of Claims: 50
CLMN
       Exemplary Claim: 1
\mathsf{ECL}
       2 Drawing Page(s)
DRWN
LN.CNT 1867
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
```

An antioxidant compound is disclosed. The compound is characterized by AΒ (a) a peptide including at least three amino acid residues of which at least two are cysteine residues, each having a readily oxidizable sulfhydryl group for effecting antioxidation; and at least two peptide bonds, each being cleavable by at least one intracellular peptidase; and (b) a first hydrophobic or non-charged moiety being attached to an amino terminal of the peptide via a first bond and a second hydrophobic or non-charged moiety being attached to a carboxy terminal of the peptide via a second bond, the first hydrophobic or non-charged moiety and the second hydrophobic or non-charged moiety are selected so as to provide the antioxidant compound with membrane miscibility properties for permitting the antioxidant compound to cross cellular membranes; wherein cleavage of the at least two peptide bonds by the at least one intracellular peptidase results in generation of a plurality of antioxidant species, each including one of the cysteine residues having the readily oxidizable sulfhydryl group and which is also active in effecting antioxidation, thereby providing for a plurality of different antioxidant species acting in synergy in exerting antioxidation.

```
ANSWER 7 OF 11 USPATFULL on STN
L3
AN
       2003:120316 USPATFULL
       Device and method for taking biological sample
TI
       Rastorgoueff, Michel, La Celle Saint Cloud, FRANCE
IN
       Deslys, Jean-Philippe, Le Chesnay, FRANCE
       Comoy, Emmanuel, Saint Aubin, FRANCE
ΡI
       US 2003082797
                               20030501
                          A1
                               20020614 (10)
AΙ
       US 2002-168005
                          A1
       WO 2000-FR3476
                               20001212
PRAI
       FR 1999-16018
                           19991217
       Utility
DT
```

```
Number of Claims: 14
CLMN
       Exemplary Claim: 1
ECL
       4 Drawing Page(s)
DRWN
LN.CNT 695
       The invention relates to a device for taking a soft biological sample
AB
       and a method for the implementation thereof. The device comprises a
       hollow cylindrical body (10) with two openings (10A, 10B), one at each
       end, wherein a piston (12) with a rod (14) is inserted via a first end
       and the piston and rod unit can be displaced back and forth inside the
       hollow cylindrical body (10). The opening of the second end (10B) of the
       hollow cylindrical body (10) has a cutting edge (10B). Said second end
       comprises a cutting wire which is disposed across the opening.
     ANSWER 8 OF 11 USPATFULL on STN
L3
       2003:183843 USPATFULL
AN
       Compounds and methods for diagnosing and treating amyloid-related
TI
       conditions
       Raub, Thomas J., Kalamazoo, MI, United States
IN
       Sawada, Geri A., Portage, MI, United States
       Tanis, Steven P., Kalamazoo, MI, United States
       Fici, Gregory J., Kalamazoo, MI, United States
       Buhl, Allen Edwin, Portage, MI, United States
       Carter, Donald Bainbridge, Kalamazoo, MI, United States
       Bandiera, Tiziano, Gambolo-Pavia, ITALY
       Lansen, Jacqueline, Milan, ITALY
       Pellerano, Cesare, Siena, ITALY
       Savini, Luisa, Siena, ITALY
       Pharmacia & Upjohn Company, Kalamazoo, MI, United States (U.S.
PA
       corporation)
       US 6589504
PI
                               20030708
                          В1
ΑI
       US 2000-667357
                               20000922 (9)
       US 2000-234611P
                           20000922 (60)
PRAI
       Utility
\operatorname{DT}
FS
       GRANTED
      Primary Examiner: Padmanabhan, Sreeni; Assistant Examiner: Willis,
EXNAM
       Michael A.
       Pharmacia & Upjohn, Darnley, Jr., James D.
LREP
       Number of Claims: 19
       Exemplary Claim: 1
ECL
       0 Drawing Figure(s); 0 Drawing Page(s)
DRWN
LN.CNT 1195
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The invention provides methods for diagnosing and treating
AB
       amyloid-related conditions and compounds useful for the same. The
       invention provides for detecting, imaging, monitoring, diagnosing, and
       treating conditions characterized by the binding or aggregation of
       amyloid fibrils. More particularly, the invention relates to using
       quinolinehydrazone compounds for diagnosing and treating amyloidotic
       conditions and also as an antioxidant.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L3
     ANSWER 9 OF 11 USPATFULL on STN
AN
       2002:157046 USPATFULL
       Diagnosis of spongiform encephalopathy
TI
IN
       Collinge, John, London, UNITED KINGDOM
                               20020627
PI
       US 2002081645
                          A1
       US 2001-778926
                               20010206 (9)
AI
                          A1
RLI
       Continuation of Ser. No. US 1999-291215, filed on 14 Apr 1999, ABANDONED
PRAI
       GB 1996-21469
                           19961015
```

MERCHANT & GOULD PC, P.O. BOX 2903, MINNEAPOLIS, MN, 55402-0903

FS

LREP

APPLICATION

GB 1996-21885

19961021

```
DT
       Utility
       APPLICATION
FS
LREP
       HALE AND DORR, LLP, 60 STATE STREET, BOSTON, MA, 02109
CLMN
       Number of Claims: 34
       Exemplary Claim: 1
ECL
       9 Drawing Page(s)
DRWN
LN.CNT 1149
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention relates to a method for typing a sample
AB
       of a prion or spongiform encephalopathy disease, a
       kit suitable for use in such a typing method, a method for identifying
       infection in an animal and/or tissue of bovine spongiform encephalopathy
       (BSE), a method for assessing and/or predicting the susceptibility of an
       animal to BSE, a kit for use in such an assessment and/or prediction
       method, a method for the treatment of a prion disease, and compounds
       suitable for such a method.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L3
                      WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
     ANSWER 10 OF 11
     2000-086592 [07]
                        WPIDS
AN
DNC
     C2000-024079
TI
     Treating disease associated with amyloid deposition such as Alzheimer's
     disease, rheumatoid arthritis, tuberculosis, Medullary carcinoma of
     thyroid, atrial amyloid etc.
DC
     B04 D16
     HRNCIC, R; SOLOMON, A; WALL, J S
IN
     (UYTE-N) UNIV TENNESSEE RES CORP; (UYTE-N) UNIV TENNESSEE RES FOUND;
PA
     (HRNC-I) HRNCIC R; (SOLO-I) SOLOMON A; (WALL-I) WALL J S
CYC
     87
                     A1 19991125 (200007)* EN
PI
     WO 9960024
                                                 34
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
            OA PT SD SE SL SZ UG ZW
         W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB
            GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU
            LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
            TT UA UG UZ VN YU ZA ZW
                     A 19991206 (200019)
     AU 9940075
                     A1 20010228 (200113)
     EP 1078005
                                           \mathbf{E}\mathbf{N}
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            RO SE SI
                     A 20010625 (200173)
     KR 2001052374
                     W 20020528 (200238)
                                                 37
     JP 2002515235
     CN 1344275
                     A 20020410 (200249)
                     A 20020828 (200264)
                                                 55
     ZA 2000007811
                     A1 20030807 (200358)
     US 2003147882
     NZ 507727
                     A 20031128 (200382)
                     A1 20030401 (200415)
     MX 2000011348
     WO 9960024 A1 WO 1999-US11200 19990521; AU 9940075 A AU 1999-40075
ADT
     19990521; EP 1078005 A1 EP 1999-923260 19990521, WO 1999-US11200 19990521;
     KR 2001052374 A KR 2000-713040 20001120; JP 2002515235 W WO 1999-US11200
     19990521, JP 2000-549642 19990521; CN 1344275 A CN 1999-808844 19990521;
     ZA 2000007811 A ZA 2000-7811 20001221; US 2003147882 A1 Provisional US
     1998-86198P 19980521, US 1999-316387 19990521; NZ 507727 A NZ 1999-507727
     19990521, WO 1999-US11200 19990521; MX 2000011348 A1 WO 1999-US11200
     19990521, MX 2000-11348 20001117
     AU 9940075 A Based on WO 9960024; EP 1078005 A1 Based on WO 9960024; JP
\mathtt{FDT}
     2002515235 W Based on WO 9960024; NZ 507727 A Based on WO 9960024; MX
     2000011348 Al Based on WO 9960024
PRAI US 1998-86198P
                          19980521; US 1999-316387
                                                          19990521
     2000-086592 [07]
AN
                        WPIDS
AΒ
          9960024 A UPAB: 20021105
     NOVELTY - Treating an amyloid deposition disease by administering
     immunoglobulin polypeptide or fragment (I) that binds to amyloid fibril,
```

is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) (I) binding to amyloid fibril and enhancing cellular immune response in amyloid fibril deposits associated diseases;
 - (2) pharmaceutical composition comprising (I);
- (3) nucleic acid molecule (II) encoding polypeptide comprising hypervariable region of (I);
 - (4) host cell comprising (II) and
 - (5) producing (I) by culturing (II).

ACTIVITY - Antinflammatory; nootropic; neuroprotective; antidiabetic; Tuberculostatic; antirheumatic; antiarthritic; cytostatic. 0.1mg of one of three antibodies kappal, kappa4 or lambda 8 was injected into mouse which had already been introduced with amyloidoma. The kappal and kappa4 reagents resulted in the complete removal by the host of most amyloid fibril species tested within 7 days. The lambda 8 reagent which was reactive in certain instances in both in vitro studies increased the resolution of amyloidomas by upto 10% in vivo experiments.

MECHANISM OF ACTION - The antibody binds to amyloid fibril.

USE - For treating amyloid deposit associated disorders, such as Alzheimer's disease, type II diabetes, bovine spongiform encephalopathy, Creutzfeld-Jakob disease, scrapie, tuberculosis, rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, Familial-Mediterranean fever, plasma cell dyscrasia, Down syndrome, familial polyneuropathy, familial amyloidosis, hereditary cerebral hemorrhage, Medullary carcinoma of thyroid, atrial amyloid.

ADVANTAGE - None given.

Dwg.0/4

```
L3 ANSWER 11 OF 11 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
```

AN 1998-251422 [22] WPIDS

DNN N1998-198452 DNC C1998-078451

TI Typing of prion or spongiform

encephalopathy diseases - by comparing physiochemical properties
of samples, used to develop products for the diagnosis and treatment of
the diseases.

DC B04 C07 D16 S03

IN COLLINGE, J

PA (UNLO) IMPERIAL COLLEGE SCI TECHNOLOGY & MED; (DGED-N) D-GEN LTD; (COLL-I) COLLINGE J

CYC 80

PI WO 9816834 A1 19980423 (199822) * EN 49

RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW

AU 9747115 A 19980511 (199837) GB 2333362 A 19990721 (199931)

EP 934531 A1 19990811 (199936) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

ES 2134749 T1 19991016 (199950)

JP 2001503141 W 20010306 (200116) 46

GB 2354946 A 20010411 (200122)

GB 2355074 A 20010411 (200122) GB 2333362 B 20010516 (200128)

GB 2354946 B 20010516 (200128)

NZ 335290 A 20010831 (200157) US 2002081645 A1 20020627 (200245)

ADT WO 9816834 A1 WO 1997-GB2843 19971015; AU 9747115 A AU 1997-47115 19971015; GB 23333362 A WO 1997-GB2843 19971015, GB 1999-8649 19990415; EP 934531 A1 EP 1997-909428 19971015, WO 1997-GB2843 19971015; ES 2134749 T1 EP 1997-909428 19971015; JP 2001503141 W WO 1997-GB2843 19971015, JP

1998-518114 19971015; GB 2354946 A Derived from GB 1999-8649 19990415, GB 2001-890 20010112; GB 2355074 A Derived from GB 1999-8649 19990415, GB 2001-1033 20010115; GB 2333362 B WO 1997-GB2843 19971015, GB 1999-8649 19990415; GB 2354946 B Derived from GB 1999-8649 19990415, GB 2001-890 20010112; NZ 335290 A NZ 1997-335290 19971015, WO 1997-GB2843 19971015; US 2002081645 A1 Cont of US 1999-291215 19990414, US 2001-778926 20010206 FDT AU 9747115 A Based on WO 9816834; GB 2333362 A Based on WO 9816834; EP 934531 A1 Based on WO 9816834; ES 2134749 T1 Based on EP 934531; JP 2001503141 W Based on WO 9816834; GB 2333362 B Based on WO 9816834; NZ 335290 A Based on WO 9816834 19961015;

PRAI GB 1996-21885

19961021; GB 1996-21469

19961015

GB 1996-21496

=> => => =>

1998-251422 [22] WPIDS AN

9816834 A UPAB: 20010615 AB

> A method (A) for typing a sample of a prion (Pr) or spongiform encephalopathy (SE) disease comprising comparing the sample with a known type of Pr or SE and identifying similar physiochemical properties.

Also claimed are: (1) a kit for typing a Pr or SE sample or diagnosing a Pr or SE disease comprising a prion or encephalopathy electrophoresis gel standard and optionally a protease enzyme; (2) a method for identifying bovine SE (BSE) infection in an animal and/or tissue comprising isolating a prion protein (PrP) from the animal and/or tissue and identifying the PrP, PrP can be characterised by having similar glycoform proportions as BSE or by having 3 distinct bands on an electrophoresis gel following proteinase K digestion, the bands comprising: (i) a band of highest mol. weight in the greatest proportion; (ii) a band of lowest mol. weight in the lowest proportion; and (iii) a band with a mol. weight between (i) and (ii) and of a proportion between (i) and (ii); (3) a method for assessing and/or predicting the susceptibility of an animal, in particular a human individual, to BSE or a derivative, the method comprising determining the genotype of the individual at polymorphic residue 129 of PrP; (4) a method for the prevention or treatment of a prion disease comprising the administration of a compound which inhibits the attachment of sugars to proteins and/or glycoproteins; and (5) a compound (optionally with a pharmaceutical carrier) which inhibits the attachment of sugars to proteins and/or glycoproteins for use as an active pharmaceutical agent.

USE - The products and methods can be used for the diagnosis, prediction of susceptibility to, prevention or treatment of Pr or SE diseases such as BSE or Crutzfeldt-Jakob disease (CJD). Method (3) can be used in a kit containing specific PCR primers for use in assessing and/or predicting the susceptibility of an animal, in particular a human individual, to BSE or a derivative (claimed). The compound as in (6) can be used in the manufacture of a medicament for the prevention or treatment of a prion disease (claimed). Dwg.0/9

```
=> d his
      (FILE 'HOME' ENTERED AT 09:47:16 ON 07 JUN 2004)
     FILE 'BIOSIS, MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 09:47:40 ON
     07 JUN 2004
             61 S TYP? (4A) (PRION OR SPONGIFORM) (4A) ENCEPHALOPATHY
L1
L2
             11 S L1 AND STANDARD
             11 DUP REM L2 (0 DUPLICATES REMOVED)
L3
=> s typ? (8a) (prion? or spongiform?)
           980 TYP? (8A) (PRION? OR SPONGIFORM?)
L4
=> s 14 and physicochemical
      15 L4 AND PHYSICOCHEMICAL
L5
=> s 15 not 13
            14 L5 NOT L3
=> dup rem 16
PROCESSING COMPLETED FOR L6
L7
             12 DUP REM L6 (2 DUPLICATES REMOVED)
=> s 17 and (standrd? or control?)
<----- User Break---->
SEARCH ENDED BY USER
=>
=> s 16 and (standard? or control?)
   4 FILES SEARCHED...
L8
             9 L6 AND (STANDARD? OR CONTROL?)
=> s 18 and size?
             5 L8 AND SIZE?
L9
=> d 19 bib abs 1-5
L9
     ANSWER 1 OF 5 USPATFULL on STN
      2004:35198 USPATFULL
       Concept for slurry separation and biogas production
TI
IN
       Bonde, Torben, Egaa, DENMARK
       Pedersen, Lars Jorgen, Hadsten, DENMARK
PI
                                20040212
       US 2004025715
                          A1
AI
       US 2003-362128
                                20030813 (10)
                          A1
       WO 2001-DK553
                                20010822
PRAI
       DK 2000-1246
                           20000822
       DK 2001-200000171
                           20010201
\mathbf{DT}
       Utility
FS
       APPLICATION
       BROWDY AND NEIMARK, P.L.L.C., 624 NINTH STREET, NW, SUITE 300,
LREP
       WASHINGTON, DC, 20001-5303
       Number of Claims: 157
CLMN
       Exemplary Claim: 1
\mathsf{ECL}
       6 Drawing Page(s)
DRWN
LN.CNT 3478
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention concerns an anaerobic digestion of animal manures,
AB
       energy crops and similar organic substrates. The process is capable of
       refining nutrients comprised in the digested biomass to fertilizers of
       commercial quality. The invention also provides a method for oprocessing
       animal carcasses or fractions thereof including meat and bone meal etc.,
       with the objective of providing an alternative means for processing the
```

organic waste material of animal origin while at the same time facilitating the production of fertilizers. The risk of spreading BSE prions or any other prions to animals or humans is thus substantially reduced if not eliminated. The biogas and slurry separation system according to the present ivnention is preferably integrated with the operations of animal husbandries into a total concept in which the internal and external performances of animal husbandries are optimised. The internal performances concern quality aspects related to the management of the animal houses and include industrial hygiene, animal welfare, gaseous and dust emissions and food safety. The external performances concern mainly energy production and emissions to the environment of nutrients and greenhouse gases and the sale of high quality food product.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLMN

ECL DRWN

LN.CNT 837

Number of Claims: 17

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Exemplary Claim: 1

6 Drawing Page(s)

```
L9
     ANSWER 2 OF 5 USPATFULL on STN
       2004:31201 USPATFULL
AN
       Method for producing human anti-thymocyte immunoglobulins
TI
       Tiollier, Jerome, Lyon, FRANCE
IN
       Sorlin, Laurent, Vaugneray, FRANCE
                       A1
PI
       US 2004023340
                               20040205
       US 2003-381859 A1
AI
                               20030328 (10)
       WO 2001-FR2972
                               20010925
       FR 2000-12384
PRAI
                           20000928
DT
       Utility
FS
       APPLICATION
LREP
       DORSEY & WHITNEY LLP, INTELLECTUAL PROPERTY DEPARTMENT, 4 EMBARCADERO
       CENTER, SUITE 3400, SAN FRANCISCO, CA, 94111
       Number of Claims: 14
CLMN
ECL
       Exemplary Claim: 1
       No Drawings
DRWN
LN.CNT 335
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Methods for producing improved anti-human thymocyte immunoglobulins from
AB
       specific-pathogen-free animals are provided, without the need for an
       adsorption step on human tissues and the consequent drawbacks of such a
       step.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L9
     ANSWER 3 OF 5 USPATFULL on STN
AN
       2003:71394 USPATFULL
       Device for in situ analysis and/or treatment consisting of a flexible
TI
       rod and micro system fixed at one end of said flexible rod
IN
       Pompidou, Alain, Paris, FRANCE
       Benhamou, Albert-Claude, Paris, FRANCE
PI
                               20030313
       US 2003049679
                          A1
       US 6689603
                               20040210
                          B2
       US 2002-926351
                               20020130 (9)
AI
                          A1
       WO 2001-FR803
                               20010316
PRAI
       FR 2000-3474
                           20000317
DT
       Utility
       APPLICATION
FS
LREP
       OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C., 1940 DUKE STREET,
       ALEXANDRIA, VA, 22314
```

AB This invention concerns an apparatus for chemical or biological analysis or treatment in situ comprising (i) a microsystem for investigation of a substrate and/or for delivery of active agents in a substrate and (ii) a

flexible rod to one end of which the microsystem is attached and the other end of which is intended for the control of said microsystem. The microsystem is advantageously of the type comprising a support on the surface of which predefined regions are arrayed, each containing different chemical or biological substances for investigation or treatment of the substrate where the microsystem is brought in contact thanks to the flexible rod.

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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L9
     ANSWER 4 OF 5 USPATFULL on STN
AN
       2002:243082 USPATFULL
       Prion isomers, methods of making, methods of using, and compositions and
TI
       products comprising prion isomers
       Chang, Jui-Yoa, Houston, TX, UNITED STATES
IN
      Lu, Bao-Yuan, Houston, TX, UNITED STATES
PI
      US 2002132268
                          A1
                               20020919
                               20011219 (10)
AΙ
      US 2001-25976
                          A1
PRAI
      US 2000-258576P 20001227 (60)
      Utility
DT
FS
      APPLICATION
      Gilbreth & Associates, P.C., PO Box 2428, Bellaire, TX, 77402-2428
LREP
CLMN
      Number of Claims: 50
ECL
      Exemplary Claim: 1
       6 Drawing Page(s)
DRWN
LN.CNT 1284
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Prion peptides exhibiting structural isomerism to wild-
AB
       type prion peptide are disclosed. The invention
       further discloses methods of making prion isomers, compositions
       comprising prion isomers, and compositions and products comprising
       antibody to a prion isomer. Methods for screening a patient for a
      neuro-degenerative disease, and methods for treating a patient afflicted
      with a neuro-degenerative disease are also disclosed.
    ANSWER 5 OF 5 USPATFULL on STN
       2001:155824 USPATFULL
      Biocompatible polymers, process for their preparation and compositions
```

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

```
L9
AN
TI
       containing them
       Barritault, Denis, Paris, France
IN
       Caruelle, Jean-Pierre, Saint-Maur-des-Fosses, France
PI
       US 2001021758
                           A1
                                20010913
       US 6689741
                                20040210
                           B2
\mathsf{AI}
                                20010119 (9)
       US 2001-765788
                           A1
       Continuation of Ser. No. WO 1999-FR1774, filed on 20 Jul 1999, UNKNOWN
RLI
PRAI
       FR 1998-9309
                            19980721
DT
       Utility
FS
       APPLICATION
LREP
       IP Department, Schnader Harrison Segal & Lewis, 36th Floor, 1600 Market
       Street, Philadelphia, PA, 19103
       Number of Claims: 60
CLMN
\mathsf{ECL}
       Exemplary Claim: 1
       30 Drawing Page(s)
DRWN
LN.CNT 2510
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB
       A biocompatible polymer constituted by a sequence of identical or
       different components of the general formula (I): A.sub.aX.sub.xY.sub.y,
```

in which A represents a monomer, X represents a carboxyl group fixed on

substitution rate of the set of monomers A by the groups X, y represents

a monomer A, Y represents a sulfate or sulfonate group fixed on a

monomer A; a represents the number of monomers A, x represents the

the substitution rate of the set of monomers A by the groups Y. The

invention also pertains to the pharmaceutical or diagnostic compositions containing at least one polymer of general formula (I).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=>

```
=> s typ? (4a) prion?
           565 TYP? (4A) PRION?
L11
=> s l11 and PrP? *3a) type?
UNMATCHED RIGHT PARENTHESIS '*3A) TYPE?'
The number of right parentheses in a query must be equal to the
number of left parentheses.
=> s 111 and PrP? (3a) type?
L12
           133 L11 AND PRP? (3A) TYPE?
=> s 112 and size?
            28 L12 AND SIZE?
L13
=> s 113 and ratio?
L14
            13 L13 AND RATIO?
=> s l14 and qlycoform?
             3 L14 AND GLYCOFORM?
L15
=> d 115 bib abs 1-3
L15
     ANSWER 1 OF 3 USPATFULL on STN
AN
       2003:70964 USPATFULL
TI
       Agent
       Weissmann, Charles, London, UNITED KINGDOM
IN
       Enari, Masato, Tokyo, JAPAN
       US 2003049249
PI
                          A1
                                20030313
AΙ
       US 2001-985164
                          A1
                               20011101 (9)
PRAI
       GB 2001-22162
                           20010913
       Utility
DT
FS
       APPLICATION
       Michele M. Simkin, FOLEY & LARDNER, Washington Harbour, 3000 K Street,
LREP
       N.W., Suite 500, Washington, DC, 20007-5109
       Number of Claims: 8
CLMN
       Exemplary Claim: 1
ECL
       4 Drawing Page(s)
DRWN
LN.CNT 1557
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The invention relates to a method of treating or preventing prion
       infection in a subject comprising administering to said subject a
       therapeutically effective amount of an agent wherein said agent cleaves
       PrPC.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 2 OF 3 USPATFULL on STN
L15
       2002:157046 USPATFULL
AN
       Diagnosis of spongiform encephalopathy
TI
       Collinge, John, London, UNITED KINGDOM
IN
       US 2002081645
PI
                          A1
                                20020627
                                20010206 (9)
AI
                          A1
       US 2001-778926
       Continuation of Ser. No. US 1999-291215, filed on 14 Apr 1999, ABANDONED
RLI
       GB 1996-21469
                           19961015
PRAI
                           19961021
       GB 1996-21885
       Utility
DT
       APPLICATION
FS
LREP
       HALE AND DORR, LLP, 60 STATE STREET, BOSTON, MA, 02109
       Number of Claims: 34
CLMN
       Exemplary Claim: 1
\mathsf{ECL}
       9 Drawing Page(s)
DRWN
LN.CNT 1149
```

The present invention relates to a method for **typing** a sample of a **prion** or spongiform encephalopathy disease, a kit suitable for use in such a typing method, a method for identifying infection in an animal and/or tissue of bovine spongiform encephalopathy (BSE), a method for assessing and/or predicting the susceptibility of an animal to BSE, a kit for use in such an assessment and/or prediction method, a method for the treatment of a prion disease, and compounds suitable for such a method.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 3 OF 3 USPATFULL on STN

AN 1999:170827 USPATFULL

TI Detecting cow, sheep and human prions in a sample and transgenic mice used for same

IN Prusiner, Stanley B., San Francisco, CA, United States Scott, Michael R., San Francisco, CA, United States Telling, Glenn C., San Francisco, CA, United States

PA The Regents of the University of California, Oakland, CA, United States (U.S. corporation)

PI US 6008435

19991228

AI US 1997-935363

19970922 (8)

Continuation-in-part of Ser. No. US 1996-692892, filed on 30 Jul 1996, now patented, Pat. No. US 5792901 which is a continuation-in-part of Ser. No. US 1995-521992, filed on 31 Aug 1995, now patented, Pat. No. US 5908969 which is a continuation-in-part of Ser. No. US 1995-509261, filed on 31 Jul 1995, now patented, Pat. No. US 5763740 which is a continuation-in-part of Ser. No. US 1994-242188, filed on 13 May 1994, now patented, Pat. No. US 5565186, issued on 15 Oct 1996

DT Utility

FS Granted

EXNAM Primary Examiner: Campell, Bruce R.; Assistant Examiner: Baker, Anne-Marie

LREP Bozicevic, Field & Francis LLP

CLMN Number of Claims: 10

ECL Exemplary Claim: 1
DRWN No Drawings

LN.CNT 1676

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Transgenic animals are produced which animals have (1) their endogenous PrP gene ablated; and (2) have an exogenous PrP gene from a genetically diverse animal. The transgenic animal is preferably a mouse, rat or hamster with mice being particularly preferred. The exogenous PrP gene is preferably from a sheep, cow, or pig with cow PrP genes being particularly preferred. When a mouse of the invention is inoculated with a sample containing prions which generally only infects a genetically diverse species (e.g. a cow) the mouse will become ill within about 250 days or less. Methods of producing the transgenic animals are disclosed including (1) microinjecting a mouse egg (having an ablated endogenous PrP gene) with a bovine PrP gene, or (2) breeding a mouse with an ablated PrP gene with a mouse with a bovine PrP gene. Mice produced are used to test samples for the presence of prions which generally only infect cows.

```
=> s typ? (4a) prion? and known (3a) PrP?
L16
            45 TYP? (4A) PRION? AND KNOWN (3A) PRP?
=> s l16 and size?
L17
            29 L16 AND SIZE?
=> s l17 and ratio?
L18
            15 L17 AND RATIO?
=> dup rem 118
PROCESSING COMPLETED FOR L18
             15 DUP REM L18 (0 DUPLICATES REMOVED)
L19
=> d l19 bib abs 1-15
     ANSWER 1 OF 15 USPATFULL on STN
L19
       2004:70108 USPATFULL
AN
       Method for detecting prions
TI
       Prusiner, Stanley B., San Francisco, CA, UNITED STATES
IN
       Safar, Jiri, Walnut Creek, CA, UNITED STATES
       The Regents of the University of California (U.S. corporation)
PA
PI
       US 2004053335
                          A1
                               20040318
       US 2003-641663
                          A1
                               20030814 (10)
AI
       Continuation of Ser. No. US 2000-699033, filed on 27 Oct 2000, GRANTED,
RLI
       Pat. No. US 6620629 Continuation-in-part of Ser. No. US 1999-235372,
       filed on 20 Jan 1999, GRANTED, Pat. No. US 6221614 Continuation-in-part
       of Ser. No. US 1998-151057, filed on 10 Sep 1998, ABANDONED
       Continuation-in-part of Ser. No. US 1998-26957, filed on 20 Feb 1998,
       ABANDONED Continuation-in-part of Ser. No. US 1997-804536, filed on 21
       Feb 1997, GRANTED, Pat. No. US 5891641
       Utility
\mathtt{DT}
FS
       APPLICATION
       BOZICEVIC, FIELD & FRANCIS LLP, 200 MIDDLEFIELD RD, SUITE 200, MENLO
LREP
       PARK, CA, 94025
       Number of Claims: 22
CLMN
       Exemplary Claim: 1
\mathsf{ECL}
       4 Drawing Page(s)
DRWN
LN.CNT 1328
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention provides assays for identifying the levels of both
       protease sensitive and protease resistant conformers of PrP.sup.Sc in a
       sample. In a preferred embodiment, the assay comprises determining
       levels of total PrP.sup.Sc in a sample, subjecting the PrP.sup.Sc
       fraction to treatment with a protease that selectively hydrolyzes the
       protease sensitive PrP.sup.Sc (sPrP.sup.Sc) conformers, and quantifying
       the levels of sPrP.sup.Sc in the sample. The ability to detect
       sPrP.sup.Sc allows early detection of prions, since the PrP.sup.Sc in
       easily accessible biological samples such as blood is predominantly
       sPrP.sup.Sc. The ratio of sPrP.sup.Sc to rPrP.sup.Sc also
       allows the identification of a particular prion strain in an infected
       sample.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 2 OF 15 USPATFULL on STN
L19
       2004:69606 USPATFULL
AN
       Sodium dodecyl sulfate compositions for inactivating prions
TI
       Prusiner, Stanley B., San Francisco, CA, UNITED STATES
IN
       Supattapone, Surachai, Hanover, NH, UNITED STATES
       The Regents of the University of California (U.S. corporation)
PA
```

US 2004052833

US 2003-641687

PI

AI

RLI

A1

Α1

20040318

20030814 (10)

Continuation of Ser. No. US 2002-56222, filed on 22 Jan 2002, PENDING

Continuation-in-part of Ser. No. US 2001-904178, filed on 11 Jul 2001, PENDING Continuation-in-part of Ser. No. US 2000-699284, filed on 26 Oct 2000, PENDING Continuation-in-part of Ser. No. US 2000-494814, filed on 31 Jan 2000, GRANTED, Pat. No. US 6322802 Continuation-in-part of Ser. No. US 1999-447456, filed on 22 Nov 1999, GRANTED, Pat. No. US 6331296 Continuation-in-part of Ser. No. US 1999-322903, filed on 1 Jun 1999, GRANTED, Pat. No. US 6214366 Continuation-in-part of Ser. No. US 1999-235372, filed on 20 Jan 1999, GRANTED, Pat. No. US 6221614 Continuation-in-part of Ser. No. US 1998-151057, filed on 10 Sep 1998, ABANDONED Continuation-in-part of Ser. No. US 1998-26957, filed on 20 Feb 1998, ABANDONED Continuation-in-part of Ser. No. US 1997-804536, filed on 21 Feb 1997, GRANTED, Pat. No. US 5891641

DT Utility

FS APPLICATION

LREP BOZICEVIC, FIELD & FRANCIS LLP, 200 MIDDLEFIELD RD, SUITE 200, MENLO PARK, CA, 94025

CLMN Number of Claims: 38
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)

LN.CNT 3478

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

An antiseptic composition useful in destroying the infectivity of infectious proteins such as prions is disclosed. The antiseptic composition is preferably maintained at either a low pH of 4.0 or less or a high pH of 10.0 or more either of which allows for an environment under which the active component (which is preferably sodium dodecyl sulfate) destroys infectivity. The composition may be added to blood, blood products, collagen, tissues and organs prior to transplantation. The composition also may be added to livestock feed to denature any prions in the livestock. Methods of denaturing infectious proteins are also disclosed which method can use but do not require higher temperatures and long period of exposure.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L19 ANSWER 3 OF 15 USPATFULL on STN

AN 2004:24715 USPATFULL

TI Methods and compositions for detection of bovine spongiform encephalopathy and variant creutzfeldt-jacob disease

IN Green, Larry R., Tacoma, WA, UNITED STATES

PI US 2004018554 A1 20040129

AI US 2002-128608 A1 20020422 (10) PRAI US 2001-291477P 20010515 (60)

PRAI US 2001-29

FS APPLICATION

LREP Richard A. Nakashima, BLAKELY, SOKOLOFF, TAYLOR & ZAFMAN LLP, 7th Floor, 12400 Wilshire Boulevard, Los Angeles, CA, 90025

CLMN Number of Claims: 29

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1728

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention discloses compositions and methods for the detection of infective agents (prions) associated with transmissible spongiform encephalopathies. More particularly, the present invention involves compositions and methods for detection and diagnosis of "mad cow" disease and vCJD. In certain embodiments, prions are treated to remove bound lipids before immunodetection. In other embodiments, hydrophobic probes are used to collect prions from oral or anal tissue. Preferred embodiments of the invention involve the use of arrays of binding moieties, such as antibodies, with varying degrees of affinity and specificity for the infective agent. The presence of prions in biological samples may be determined by the pattern of binding of infective agent to the array. The prions may be distinguished from other

proteins of similar or identical amino acid sequence, but different secondary, tertiary or quaternary structure, by the different patterns of binding to the array.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. L19 ANSWER 4 OF 15 USPATFULL on STN AN2003:206867 USPATFULL Antibodies specific for ungulate PrP TIINPrusiner, Stanley B., San Francisco, CA, UNITED STATES Safar, Jiri G., Walnut Creek, CA, UNITED STATES Williamson, R. Anthony, San Diego, CA, UNITED STATES Burton, Dennis R., La Jolla, CA, UNITED STATES 20030731 PIUS 2003143224 A1 AIUS 2003-355780 A1 20030130 (10) RLIContinuation of Ser. No. US 2000-627218, filed on 27 Jul 2000, GRANTED, Pat. No. US 6537548 Utility DTFS APPLICATION BOZICEVIC, FIELD & FRANCIS LLP, 200 MIDDLEFIELD RD, SUITE 200, MENLO LREP PARK, CA, 94025 Number of Claims: 20 CLMN Exemplary Claim: 1 ECL 9 Drawing Page(s) DRWN LN.CNT 2123 CAS INDEXING IS AVAILABLE FOR THIS PATENT. The present invention provides antibodies that specifically bind with a ABhigh degree of binding affinity to a native ungulate PrP.sup.C and/or a denatured ungulate PrP.sup.Sc, but not to a native ungulate PrP.sup.Sc. Preferred antibodies find native bovine PrP.sup.C and treated PrP.sup.Sc but not native bovine PrP.sup.Sc and can be used in an assay to determine if a sample is infected with infectious prions, i.e. PrP.sup.Sc.

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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L19
     ANSWER 5 OF 15 USPATFULL on STN
\mathbf{N}\mathbf{A}
       2003:4268 USPATFULL
       Sodium dodecyl sulfate compositions for inactivating prions
TI
       Prusiner, Stanley B., San Francisco, CA, UNITED STATES
IN
       Supattapone, Surachai, Hanover, NH, UNITED STATES
       US 2003004312
PI
                                20030102
                          A1
       US 6720355
                          B2
                                20040413
       US 2002-56222
AI
                          Α1
                                20020122 (10)
       Continuation-in-part of Ser. No. US 2001-904178, filed on 11 Jul 2001,
RLI
       PENDING Continuation-in-part of Ser. No. US 2000-699284, filed on 26 Oct
       2000, PENDING Continuation-in-part of Ser. No. US 2000-494814, filed on
       31 Jan 2000, GRANTED, Pat. No. US 6322802 Continuation-in-part of Ser.
       No. US 1999-447456, filed on 22 Nov 1999, GRANTED, Pat. No. US 6331296
       Continuation-in-part of Ser. No. US 1999-322903, filed on 1 Jun 1999,
       GRANTED, Pat. No. US 6214366 Continuation-in-part of Ser. No. US
       1999-235372, filed on 20 Jan 1999, GRANTED, Pat. No. US 6221614
       Continuation-in-part of Ser. No. US 1998-151057, filed on 10 Sep 1998,
       ABANDONED Continuation-in-part of Ser. No. US 1998-26957, filed on 20
       Feb 1998, ABANDONED Continuation-in-part of Ser. No. US 1997-804536,
       filed on 21 Feb 1997, GRANTED, Pat. No. US 5891641
DT
       Utility
```

FS APPLICATION

LREP BOZICEVIC, FIELD & FRANCIS LLP, 200 MIDDLEFIELD RD, SUITE 200, MENLO PARK, CA, 94025

Number of Claims: 38 CLMN Exemplary Claim: 1 ECL DRWN 12 Drawing Page(s)

LN.CNT 3471

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

An antiseptic composition useful in destroying the infectivity of AB infectious proteins such as prions is disclosed. The antiseptic composition is preferably maintained at either a low pH of 4.0 or less or a high pH of 10.0 or more either of which allows for an environment under which the active component (which is preferably sodium dodecyl sulfate) destroys infectivity. The composition may be added to blood, blood products, collagen, tissues and organs prior to transplantation. The composition also may be added to livestock feed to denature any prions in the livestock. Methods of denaturing infectious proteins are also disclosed which method can use but do not require higher temperatures and long period of exposure.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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ANSWER 6 OF 15 USPATFULL on STN
L19
       2003:246844 USPATFULL
AN
       Method for detecting prions
{f T}{f I}
       Prusiner, Stanley B., San Francisco, CA, United States
IN
       Safar, Jiri, Concord, CA, United States
       The Regents of the University of California, Oakland, CA, United States
PA
       (U.S. corporation)
PI
       US 6620629
                          B1
                                20030916
AΙ
       US 2000-699033
                                20001027 (9)
       Continuation-in-part of Ser. No. US 1999-235372, filed on 20 Jan 1999,
RLI
       now patented, Pat. No. US 6221614 Continuation-in-part of Ser. No. US
       1998-151057, filed on 10 Sep 1998, now abandoned Continuation-in-part of
       Ser. No. US 1998-26957, filed on 20 Feb 1998, now abandoned
       Continuation-in-part of Ser. No. US 1997-804536, filed on 21 Feb 1997,
       now patented, Pat. No. US 5891641
       Utility
DT
FS
       GRANTED
       Primary Examiner: Scheiner, Laurie; Assistant Examiner: Parkin, Jeffrey
EXNAM
       Bozicevic, Karl, Bozicevic, Field & Francis LLP
LREP
```

Number of Claims: 13 CLMN

Exemplary Claim: 1 ECL

4 Drawing Figure(s); 4 Drawing Page(s) DRWN

LN.CNT 1459

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention provides assays for identifying the levels of both protease sensitive and protease resistant conformers of PrP.sup.Sc in a sample. In a preferred embodiment, the assay comprises determining levels of total PrP.sup.Sc in a sample, subjecting the PrP.sup.Sc fraction to treatment with a protease that selectively hydrolyzes the protease sensitive PrP.sup.Sc (sPrP.sup.Sc) conformers, and quantifying the levels of sPrP.sup.Sc in the sample. The ability to detect sPrP.sup.Sc allows early detection of prions, since the PrP.sup.Sc in easily accessible biological samples such as blood is predominantly sPrP.sup.Sc. The ratio of sPrP.sup.Sc to rPrP.sup.Sc also allows the identification of a particular prion strain in an infected sample.

```
ANSWER 7 OF 15 USPATFULL on STN
L19
AN
       2003:81453 USPATFULL
       Antibodies specific for ungulate PrP
TI
       Prusiner, Stanley B., San Francisco, CA, United States
IN
       Safar, Jiri, Concord, CA, United States
       Williamson, R. Anthony, San Diego, CA, United States
       Burton, Dennis R., La Jolla, CA, United States
       The Regents of the University of California, Oakland, CA, United States
PA
       (U.S. corporation)
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The Scripps Research Institute, La Jolla, CA, United States (U.S.
       corporation)
       US 6537548
                          B1
                                20030325
PI
       US 2000-627218
                                20000727 (9)
AΙ
       Utility
DT
FS
       GRANTED
      Primary Examiner: Housel, James; Assistant Examiner: Winkler, Ulrike
EXNAM
       Bozicevic, Karl, Bozicevic, Field & Francis LLP
LREP
       Number of Claims: 8
CLMN
       Exemplary Claim: 1
ECL
       13 Drawing Figure(s); 9 Drawing Page(s)
DRWN
LN.CNT 2073
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention provides antibodies that specifically bind with a
AB
       high degree of binding affinity to a native ungulate PrP.sup.C and/or a
       denatured ungulate PrP.sup.Sc, but not to a native ungulate PrP.sup.Sc.
       Preferred antibodies find native bovine PrP.sup.C and treated PrP.sup.Sc
       but not native bovine PrP.sup.Sc and can be used in an assay to
       determine if a sample is infected with infectious prions, i.e.
       PrP.sup.Sc.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L19
     ANSWER 8 OF 15 USPATFULL on STN
AN
       2002:157046 USPATFULL
       Diagnosis of spongiform encephalopathy
ΤI
       Collinge, John, London, UNITED KINGDOM
IN
PI
       US 2002081645
                          A1
                                20020627
                                20010206 (9)
       US 2001-778926
                          A1
AΙ
       Continuation of Ser. No. US 1999-291215, filed on 14 Apr 1999, ABANDONED
RLI
PRAI
       GB 1996-21469
                            19961015
       GB 1996-21885
                           19961021
       Utility
\operatorname{DT}
FS
       APPLICATION
       HALE AND DORR, LLP, 60 STATE STREET, BOSTON, MA, 02109
LREP
       Number of Claims: 34
CLMN
       Exemplary Claim: 1
\mathsf{ECL}
       9 Drawing Page(s)
DRWN
LN.CNT 1149
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention relates to a method for typing a sample
       of a prion or spongiform encephalopathy disease, a kit
       suitable for use in such a typing method, a method for identifying
       infection in an animal and/or tissue of bovine spongiform encephalopathy
       (BSE), a method for assessing and/or predicting the susceptibility of an
       animal to BSE, a kit for use in such an assessment and/or prediction
       method, a method for the treatment of a prion disease, and compounds
       suitable for such a method.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L19
     ANSWER 9 OF 15 USPATFULL on STN
AN
       2002:78467 USPATFULL
       Mammalian proteins; related reagents and methods
\mathtt{TI}
       Bazan, J. Fernando, Palo Alto, CA, UNITED STATES
IN
                                20020411
\mathtt{PI}
       US 2002042122
                          A1
                                20001220 (9)
       US 2000-745003
AΙ
                          A1
PRAI
                         19991223 (60)
       US 1999-172090P
DT
       Utility
FS
       APPLICATION
       DNAX RESEARCH INSTITUTE, LEGAL DEPARTMENT, 901 CALIFORNIA AVENUE, PALO
LREP
       ALTO, CA, 94304
CLMN
       Number of Claims: 20
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ECL

Exemplary Claim: 1

LN.CNT 2359 CAS INDEXING IS AVAILABLE FOR THIS PATENT. Mammalian polypeptides, isolated proteins, and fragments thereof AΒ including the polynucleotides encoding them. Antibodies, both polyclonal and monoclonal, are also provided. Methods of using the compositions for both diagnostic and therapeutic utilities are provided. CAS INDEXING IS AVAILABLE FOR THIS PATENT. L19 ANSWER 10 OF 15 USPATFULL on STN 2002:78206 USPATFULL ANAntiseptic compositions for inactivating prions TIPrusiner, Stanley B., San Francisco, CA, UNITED STATES INSupattapone, Surachai, Hanover, NH, UNITED STATES \mathtt{PI} US 2002041859 20020411 A1 US 6719988 B2 20040413 US 2001-904178 \mathtt{AI} A120010711 (9) Continuation-in-part of Ser. No. US 2000-699284, filed on 26 Oct 2000, RLI PENDING Continuation-in-part of Ser. No. US 2000-494814, filed on 31 Jan 2000, GRANTED, Pat. No. US 6322802 Continuation-in-part of Ser. No. US 1999-447456, filed on 22 Nov 1999, PENDING Continuation-in-part of Ser. No. US 1999-322903, filed on 1 Jun 1999, GRANTED, Pat. No. US 6214366 Continuation-in-part of Ser. No. US 1999-235372, filed on 20 Jan 1999, GRANTED, Pat. No. US 6221614 Continuation-in-part of Ser. No. US 1998-151057, filed on 10 Sep 1998, ABANDONED Continuation-in-part of Ser. No. US 1998-26957, filed on 20 Feb 1998, ABANDONED Continuation-in-part of Ser. No. US 1997-804536, filed on 21 Feb 1997, GRANTED, Pat. No. US 5891641 Utility DTFS APPLICATION Karl Bozicevic, Bozicevic, Field and Francis LLP, Suite 200, 200 LREP Middlefield Road, Menlo Park, CA, 94025 Number of Claims: 22 CLMN ECLExemplary Claim: 1 DRWN 12 Drawing Page(s) LN.CNT 3354 CAS INDEXING IS AVAILABLE FOR THIS PATENT. An antiseptic composition useful in destroying the infectivity of ABinfectious proteins such as prions is disclosed. The antiseptic composition is preferably maintained at a pH of 4.0 or less which allows for an environment under which the active component destroys infectivity. The composition may be added to blood, blood products, collagen, tissues and organs prior to transplantation. The composition also may be added to livestock feed to denature any prions in the livestock. Methods of denaturing infectious proteins are also disclosed. CAS INDEXING IS AVAILABLE FOR THIS PATENT. ANSWER 11 OF 15 USPATFULL on STN L192002:3842 USPATFULL ANAssay for specific strains of multiple disease related conformations of TIa protein Prusiner, Stanley B., San Francisco, CA, UNITED STATES INSafar, Jiri G., Concord, CA, UNITED STATES Cohen, Fred E., San Francisco, CA, UNITED STATES PIUS 2002001817 Α1 20020103

20030909

20010709 (9)

Continuation of Ser. No. US 1998-151057, filed on 10 Sep 1998, PENDING

Continuation-in-part of Ser. No. US 1998-26957, filed on 20 Feb 1998, ABANDONED Continuation-in-part of Ser. No. US 1997-804536, filed on 21

B2

A1

Feb 1997, GRANTED, Pat. No. US 5891641

No Drawings

US 6617119

Utility

US 2001-901865

ΑI

DT

RLI

DRWN

FS APPLICATION

LREP Karl Bozicevic, Bozicevic, Field and Francis LLP, Suite 200, 200 Middlefield Road, Menlo Park, CA, 94025

CLMN Number of Claims: 20 ECL Exemplary Claim: 1 DRWN 19 Drawing Page(s)

LN.CNT 2676

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Assay methodology of the invention allows for: (1) determining if a sample contains a conformation of a protein which is associated with disease and the concentration and amount of such if present; (2) determining the amount of protease resistant disease related protein in a sample and by subtracting that amount from the total amount of disease related protein present determining the amount of protease sensitive disease protein in the sample; and (3) determining the strain and incubation time of a disease related protein by (i) relating the relative amounts of protease resistant and protease sensitive protein to known strains to thereby determine the strain; and (ii) plotting the concentration of protease sensitive protein on a graph of incubation time versus concentration of protease sensitive protein for known strains to predict the incubation time of an unknown strain of pathogenic protein in a sample.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L19 ANSWER 12 OF 15 USPATFULL on STN

AN 2001:88925 USPATFULL

TI Assay for disease related conformation of a protein IN Prusiner, Stanley B., San Francisco, CA, United States

Safar, Jiri G., Concord, CA, United States

PI US 2001001061 A1 20010510

AI US 2000-731419 A1 20001205 (9)

Continuation of Ser. No. US 1998-26957, filed on 20 Feb 1998, PENDING Continuation-in-part of Ser. No. US 1997-804536, filed on 21 Feb 1997, GRANTED, Pat. No. US 5891641

DT Utility
FS APPLICATION

LREP Karl Bozicevic, BOZICEVIC, FIELD & FRANCIS LLP, Suite 200, 200 Middlefield Road, Menlo Park, CA, 94025

CLMN Number of Claims: 20 ECL Exemplary Claim: 1 DRWN 14 Drawing Page(s)

LN.CNT 2288

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

An assay method is disclosed which makes it possible to determine the ABpresence of a diseased related conformation of a protein (e.g., PrP.sup.Sc or the β -sheet form of β A4) in a sample. A sample is divided into two portions and the first portion is cross-linked to a first solid support and then contacted with a labeled antibody which binds to a non-disease form of the protein with a higher degree of affinity (e.g., 4 to 30 fold higher) than to the disease form of the protein. The second portion is treated in a manner which causes any disease form of the protein to change conformation to a form with a higher binding affinity for the labeled antibody. The treated second portion is then bound to a second solid support and contacted with labeled antibody. The level of labeled antibody binding to a protein in the first and second portions is determined and the amounts measured in each are compared. The difference between the two measurements is an indication of whether the disease related conformation of the protein was present in the sample. The method can also determine the concentration of the disease related conformation and the particular strain present.

```
AN
       1999:170827 USPATFULL
       Detecting cow, sheep and human prions in a sample and transgenic mice
TI
       used for same
       Prusiner, Stanley B., San Francisco, CA, United States
IN
       Scott, Michael R., San Francisco, CA, United States
       Telling, Glenn C., San Francisco, CA, United States
       The Regents of the University of California, Oakland, CA, United States
PA
       (U.S. corporation)
       US 6008435
PI
                                19991228
ΑI
       US 1997-935363
                                19970922 (8)
       Continuation-in-part of Ser. No. US 1996-692892, filed on 30 Jul 1996,
RLI
       now patented, Pat. No. US 5792901 which is a continuation-in-part of
       Ser. No. US 1995-521992, filed on 31 Aug 1995, now patented, Pat. No. US
       5908969 which is a continuation-in-part of Ser. No. US 1995-509261,
       filed on 31 Jul 1995, now patented, Pat. No. US 5763740 which is a
       continuation-in-part of Ser. No. US 1994-242188, filed on 13 May 1994,
       now patented, Pat. No. US 5565186, issued on 15 Oct 1996
       Utility
DT
       Granted
FS
       Primary Examiner: Campell, Bruce R.; Assistant Examiner: Baker,
EXNAM
       Anne-Marie
       Bozicevic, Field & Francis LLP
LREP
       Number of Claims: 10
CLMN
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 1676
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Transgenic animals are produced which animals have (1) their endogenous
AB
       PrP gene ablated; and (2) have an exogenous PrP gene from a genetically
       diverse animal. The transgenic animal is preferably a mouse, rat or
       hamster with mice being particularly preferred. The exogenous PrP gene
       is preferably from a sheep, cow, or pig with cow PrP genes being
       particularly preferred. When a mouse of the invention is inoculated with
       a sample containing prions which generally only infects a genetically
       diverse species (e.g. a cow) the mouse will become ill within about 250
       days or less. Methods of producing the transgenic animals are disclosed
       including (1) microinjecting a mouse egg (having an ablated endogenous
       PrP gene) with a bovine PrP gene, or (2) breeding a mouse with an
       ablated PrP gene with a mouse with a bovine PrP gene. Mice produced are
       used to test samples for the presence of prions which generally only
       infect cows.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 14 OF 15 USPATFULL on STN
L19
\mathbf{AN}
       1999:121570 USPATFULL
       Nucleic acid encoding prion protein variant
TI
       Prusiner, Stanley B., San Francisco, CA, United States
IN
       Cohen, Fred E., San Francisco, CA, United States
       James, Thomas L., Nicasio, CA, United States
       Kaneko, Kiyotoshi, San Francisco, CA, United States
       The Regents of the University of California, Oakland, CA, United States
\mathbf{P}\mathbf{A}
       (U.S. corporation)
PI
       US 5962669
                               19991005
ΑI
       US 1997-868162
                               19970602 (8)
       Utility
DT
FS
       Granted
       Primary Examiner: Wax, Robert A.; Assistant Examiner: Longton, Enrique
EXNAM
       D.
LREP
       Bozicevic, KarlBozicevic, Field & Francis LLP
CLMN
       Number of Claims: 7
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ANSWER 13 OF 15 USPATFULL on STN

L19

ECL

Exemplary Claim: 1

DRWN 17 Drawing Figure(s); 15 Drawing Page(s) LN.CNT 2993

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A protein designated Prion Protein Modulator Factor (PPMF) is disclosed AB which protein is an auxiliary factor in prion replication. PPMF is primarily characterized by its ability to bind to PrP.sup.C and facilitate a conformational change from PrP.sup.C to PrP.sup.Sc. A discontinuous epitope on PrP.sup.C comprising residues 172, 215 and 219 of human PrP.sup.C binds PPMF which is encoded by a nucleotide sequence derived from an organism selected from the group consisting of cow, sheep, mouse, hamster and human. In converting PrP.sup.C to PrP.sup.Sc the PPMF forms a PrP.sup.C /PrP.sup.Sc complex and is a rate limiting compound in the formation of that complex. Molecules, including antibodies, which bind PPMF or its epitope on PrP.sup.C are useful in the treatment of prion disease. Pharmacophores of the PrP.sup.C epitope are disclosed as are useful therapeutics and pharmacophores of the PPMF surface which binds PrP.sup.C. Animals resistant to prion disease are taught as are genes for producing such animals. Assay systems are disclosed which use PPMF to amplify PrP.sup.Sc is a sample being tested.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L19 ANSWER 15 OF 15 USPATFULL on STN

AN 1999:43389 USPATFULL

TI Assay for disease related conformation of a protein

IN Prusiner, Stanley B., San Francisco, CA, United States

Safar, Jiri G., Concord, CA, United States

PA The Regents of the University of California, Oakland, CA, United States (U.S. corporation)

PI US 5891641

19990406

AI US 1997-804536

19970221 (8)

DT Utility

FS Granted

EXNAM Primary Examiner: Woodward, Michael P.; Assistant Examiner: Zeman, Mary

LREP Bozicevic, KarlBozicevic & Reed LLP

CLMN Number of Claims: 20

ECL Exemplary Claim: 1

DRWN 11 Drawing Figure(s); 6 Drawing Page(s)

LN.CNT 1990

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An assay method is disclosed which makes it possible to determine the presence of a diseased related conformation of a protein (e.g., PrP.sup.Sc) in a sample. A sample is divided into two portions and the first portion is cross-linked to a first solid support and then contacted with a labelled antibody which binds to a non-disease form of the protein with a higher degree of affinity (e.g, 4 to 30 fold higher) than to the disease form of the protein. The second portion is treated in a manner which causes any disease form of the protein to change conformation to a form with a higher binding affinity for the labelled antibody. The treated second portion is then bound to a second solid support and contacted with labelled antibody. The level of labelled antibody binding to a protein in the first and second portions is determined and the amounts measured in each are compared. The difference between the two measurements is an indication of whether the diseased related conformation of the protein was present in the sample.

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=>
-> d hie
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LN.CNT 2476

=> d his (FILE 'HOME' ENTERED AT 09:47:16 ON 07 JUN 2004) FILE 'BIOSIS, MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 09:47:40 ON 07 JUN 2004 61 S TYP? (4A) (PRION OR SPONGIFORM) (4A) ENCEPHALOPATHY L1L211 S L1 AND STANDARD 11 DUP REM L2 (0 DUPLICATES REMOVED) L3L4980 S TYP? (8A) (PRION? OR SPONGIFORM?) 15 S L4 AND PHYSICOCHEMICAL L5L614 S L5 NOT L3 12 DUP REM L6 (2 DUPLICATES REMOVED) L7 9 S L6 AND (STANDARD? OR CONTROL?) $\Gamma8$ L9 5 S L8 AND SIZE? 7 S L7 NOT L9 L10 565 S TYP? (4A) PRION? L11133 S L11 AND PRP? (3A) TYPE? L12L13 28 S L12 AND SIZE? L1413 S L13 AND RATIO? L15 3 S L14 AND GLYCOFORM? 45 S TYP? (4A) PRION? AND KNOWN (3A) PRP? L16 L1729 S L16 AND SIZE? L18 15 S L17 AND RATIO? 15 DUP REM L18 (0 DUPLICATES REMOVED) L19 => s 14 and size? 181 L4 AND SIZE? L20 => s 120 and ratio? L21105 L20 AND RATIO? => s 121 and and known (3a) PrP? MISSING TERM 'AND AND' The search profile that was entered contains a logical operator followed immediately by another operator. => s l21 and known (3a) PrP? L2217 L21 AND KNOWN (3A) PRP? => s 122 not 119 L232 L22 NOT L19 => d 123 bib abs 1-2 L23ANSWER 1 OF 2 USPATFULL on STN AN2003:72977 USPATFULL Genetically modified cows having reduced susceptibility to mad cow TIdisease Liljedahl, Monika, La Jolla, CA, UNITED STATES INAspland, Simon Eric, San Diego, CA, UNITED STATES US 2003051264 PIAl. 20030313 ΑI US 2002-209194 20020729 (10) Α1 PRAI 20010731 (60) US 2001-309222P US 2002-367091P 20020321 (60) Utility DTFS APPLICATION LREP KNOBBE MARTENS OLSON & BEAR LLP, 2040 MAIN STREET, FOURTEENTH FLOOR, IRVINE, CA, 92614 Number of Claims: 80 CLMN Exemplary Claim: 1 ECL 14 Drawing Page(s) DRWN

The present invention relates to cow cells in which a gene associated with mad cow disease has been modified to reduce susceptibility to mad cow disease, cows having reduced susceptibility to mad cow disease, nucleic acids for making such cells and cows, and products obtained from such cows. The invention also includes methods of making each of the foregoing.

L23 ANSWER 2 OF 2 USPATFULL on STN

AN 2002:339259 USPATFULL

TI Transgenic animals resistant to transmissible spongiform encephalopathies

IN Dunne, Patrick W., La Grange, TX, UNITED STATES

Piedrahita, Jorge, College Station, TX, UNITED STATES

PI US 2002194635 A1 20021219

AI US 2002-109551 A1 20020328 (10)

PRAI US 2001-280549P 20010330 (60)

DT Utility

FS APPLICATION

LREP Robert E. Hanson, Fulbright & Jaworski L.L.P., Suite 2400, 600 Congress Avenue, Austin, TX, 78701

CLMN Number of Claims: 34

ECL Exemplary Claim: 1

DRWN 8 Drawing Page(s)

LN.CNT 4210

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The invention provides modified prion-encoding genes for the creation of transgenic bovine and cervid animals resistant to transmissible spongiform encephalopathies including bovine spongiform encephalopathy (BSE). The transgenic animals homozygous for the mutant genes continue to express a functional copy of the prion-encoding gene, thereby not interfering with the normal role of the polypeptide and effectively decreasing tendency for alteration of sleep-wake cycles.